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(71) Applicant *(for all designated States except US)*: THE PROCTER & GAMBLE COMPANY [US/US]; One Procter & Gamble Plaza, Cincinnati, OH 45202 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: LUHADIYA, Ashok, Kumar, Premchand [IN/IN]; B–28, Uday Rekha CHS, Plot No. 12, Manish Nagar, Four Bunglow, Andheri(W), Mumbai 400058 (IN).

(74) Agents: REED, T., David et al.; The Procter & Gamble Company, 5299 Spring Grove Avenue, Cincinnati, OH 45217–1087 (US).

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(54) Title: CHEWABLE COMPOSITIONS CONTAINING DEXTROMETHORPHAN

(57) Abstract

Disclosed is a composition comprising dextromethorphan particles coated with a polymethacrylate copolymer, the coated particles having a particle size of less than about 150 microns. Further disclosed is a method for preparing a composition comprising dextromethorphan coated with a polymethacrylate copolymer, comprising the steps of: (a) dissolving dextromethorphan and polymethacrylate copolymer in a solvent, the ratio of the dextromethorphan to the polymethacrylate copolymer being from about 3:97 to about 50:50; (b) concentrating the dissolved solution obtained by step (a); (c) spraying the concentrated solution obtained by step (b) in a water bath maintained at from about 5 °C to about 85 °C and containing a dispersing agent to obtain a co–precipitate, the co–precipitate having a particle size of less than about 150 microns; (d) washing and drying the co–precipitate obtained by step (c). Still further disclosed are chewable tablets comprising such coated dextromethorphan compositions.

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CHEWABLE COMPOSITIONS CONTAINING DEXTROMETHORPHAN

FIELD

The present invention relates to oral dosage forms of dextromethorphan. More specifically, the present invention relates to chewable compositions containing dextromethorphan, such as tablets, in which the unpalatable taste of the dextromethorphan is masked during chewing, as well as a process for making such compositions.

BACKGROUND

Orally administered medicament compositions may be given to patients in many forms, such as liquid solutions including gels, emulsions, and suspensions; or in solid forms such as powders, granules, and tablets. Compositions administered in solid form, especially tablets, are usually intended to be swallowed whole or chewed.

Many consumers, particularly those who have difficulty swallowing a tablet (e.g., the aged or children), prefer tablets which can be readily ingested by chewing. Such people desire tablets which dissolve immediately during chewing in the mouth.

However, conventional tablets tend to produce an unacceptable mouthfeel (i.e., the overall sensation of the product in the mouth) for the user. Product attributes which tend to contribute to an unacceptable mouthfeel include bitterness (typically caused by the drug active contained in the tablet) and grittiness (i.e., the textural aspects of the granules making up the tablet, as sensed by the tongue and/or upper palate). Such unacceptable mouthfeel

properties tend to make the tablet (in chewed or unchewed form) unpalatable and leads to poor dose compliance.

Some of the drug active ingredients which tend to exhibit the undesirable characteristic of bitter taste during and/or after oral administration by e.g., swallowing and/or chewing, include e.g., acetaminophen, ampicillin, azithromycin, chlorpheniramine, cimetidine, dextromethorphan, diphenhydramine, erythromycin, ibuprofen, penicillin, phenylbutazone, psuedoephedrine, ranitidine, spironolactone, and theophylline for pharmaceutical compositions.

A variety of approaches have been developed to taste mask the bitterness of such drug active ingredients by coating with polymeric substances using conventional coating processes, such as pan coating or spray drying. See, e.g., Shen US Patent 5,552,152 (issued September 3, 1996); Hoy US Patent 5,489,436 (issued February 6, 1996); and European Patent Publication EP 293 885 B1. However, all of these preparations suffer from the disadvantage of higher particle size that gives rise to grittiness in the mouth when incorporated in a chewable tablet formulation. In addition, the spray drying coating process described in EP 293 885 B1 essentially uses highly flammable solvents, thus necessitating a flame-proof drying system and hence being dangerous to handle. Further, the residual solvent may impart its taste to the finished drug formulation. Another existing attempt to mask the bitterness of the drug active ingredient is by chemically reacting the drug with polymer. See, EP Patent Publication 266 113 B1.

Dextromethorphan is a drug active ingredient that is particularly useful for the treatment and relief of cough symptoms associated with upper respiratory illness such as the flu or the common cold. Acceptably palatable liquid oral dosage forms of dextromethorphan have been developed. Even so, it is desirable to provide a chewable solid form such as a tablet because of the added conveniences associated with tablet forms, e.g., less mess, greater ease of transport, consumer preference, and ease of administration.

Based on the foregoing, there is a need for a chewable dosage form of dextromethorphan in which the unpalatable, bitter taste of the dextromethorphan is masked during chewing and swallowing, while good mouthfeel is also provided. None of the existing art provides all of the advantages and benefits of the present invention.

SUMMARY

The present invention is directed to a composition comprising dextromethorphan particles coated with a polymethacrylate copolymer, the coated particles having a particle size of less than about 150 microns. Further disclosed is a method for preparing a composition comprising dextromethorphan coated with a polymethacrylate copolymer, comprising the steps of: (a) dissolving dextromethorphan and polymethacrylate copolymer in a solvent, the ratio of the dextromethorphan to the polymethacrylate copolymer being from about 3:97 to about 50:50; (b) concentrating the dissolved solution obtained by step (a); (c) spraying the concentrated solution obtained by step (b) in a water bath maintained at from about 5°C to about 85°C and containing a dispersing agent to obtain a co-precipitate, the co-precipitate having a particle size of less than about 150 microns; (d) washing and drying the co-precipitate obtained by step (c). Still further disclosed are chewable tablets comprising such coated dextromethorphan compositions.

These and other features, aspects, and advantages of the invention will become evident to those skilled in the art from a reading of the present disclosure.

DETAILED DESCRIPTION

While the specification concludes with claims particularly pointing out and distinctly claiming the invention, it is believed that the present invention will be better understood from the following description.

All percentages and ratios used hereinafter are by weight of total composition, unless otherwise indicated.

All measurements referred to herein are made at 25°C unless otherwise specified.

All percentages, ratios, and levels of ingredients referred to herein are based on the actual amount of the ingredient, and do not include solvents, fillers, or other materials with which the ingredient may be combined as a commercially available product, unless otherwise indicated.

All publications, patent applications, and issued patents mentioned herein are hereby incorporated in their entirety by reference. Citation of any reference

is not an admission regarding any determination as to its availability as prior art to the claimed invention.

Herein, "comprising" means that other steps and other components which do not affect the end result can be added. This term encompasses the terms "consisting of" and "consisting essentially of."

Herein, "solid tablet" means a material which has a hard shape and is made by compressing granules pre-mixed into a predetermined shape or direct compression of ingredients contained, which includes, e.g., pills, lozenges, and troches.

Herein, "paste" means a material which is in smooth liquid form having higher or lower viscosity, e.g., gel form and cream form.

Herein, "pharmaceutically acceptable" means compounds that are, within the scope of sound medical judgment, suitable for use in contact with the tissues of humans and animals without undue toxicity, irritation, allergic response, and the like, in keeping with a reasonable benefit/risk ratio, and effective for their intended use in the prophylaxis of antimicrobial infections.

A. Dextromethorphan

The compositions of the present invention include dextromethorphan. Dextromethorphan is known as an effective ingredient for the suppression and treatment of coughs due to the common cold, allergies, and other upper respiratory illnesses. It is the pharmaceutically active ingredient contained in the compositions herein and any pharmaceutically acceptable grade may be used herein.

Dextromethorphan by itself has a bitter, unpalatable taste. Alone, it is not palatable enough to be used in chewable dosage forms. Furthermore, it is believed that mere addition of flavor additives to a chewable composition containing dextromethorphan would not be sufficient to overcome this bitter taste such that the composition would be rendered acceptably palatable. Thus, it is desirable to mask this bitter taste for the chewable compositions herein by coating the dextromethorphan according to the present invention.

Taste-masking of drug actives, including dextromethorphan, by coating with lipids or polymeric substances has previously been known. Such coating has been performed by conventional methods for taste-masking such as fluidized bed coating. However, use of conventional coating methods has resulted in higher particles sizes of the coated drug active. Such higher particle

size tends to cause unacceptable mouthfeel and grittiness properties for orally administered medicament compositions, especially for those in tablet form. It is believed that such higher particle sizes of coated dextromethorphan may lead to an unacceptable gritty mouthfeel when the tablet is converted into the paste form in the mouth.

Dextromethorphan particles typically have an uncoated particle size of from about 2 microns to about 80 microns. After coating, this size range will increase, commensurate with the thickness of the coating. In preferred embodiments of the present invention, the coated particle size is not greater than 150 microns. It is believed that coated particles of such a lowered size will provide a smooth, non-gritty feeling in the mouth, especially when the tablet is converted into the paste form.

B. Coating Agent

The coating agent herein masks the inherently bitter taste of the dextromethorphan. The coating agent should be insoluble at non-acidic pH, i.e., insoluble while in the mouth, but soluble in gastric juice, i.e., soluble at pH of up to about 5.0. Such coatings are sometimes referred to as "reverse enteric" coatings. A preferred coating agent herein is an acrylic resin copolymer, cationic in character, based on dimethylaminoethyl methacrylate and neutral methacrylic acid esters, i.e., a polymethacrylate copolymer. A suitable commercially available acrylic resin copolymer is sold by Röhm Pharma GmbH under the trade name "Eudragit E". Especially suitable for use herein is Eudragit E 100, which is supplied as a solid substance having the appearance of light yellow granules.

Preferably the ratio of the coating agent to the dextromethorphan herein is from about 3:97 to about 50:50 w/w.

C. Method of Coating the Dextromethorphan

The coating of the dextromethorphan with the coating agent according to the present invention is preferably performed by a co-precipitation method. The dextromethorphan and the coating agent are dissolved in an organic solvent such as ethyl alcohol in a hot water bath with continuous stirring to facilitate quick dissolution of the coating agent. The mixture is then concentrated to about 40% of its initial volume by evaporating the organic solvent. The concentrated mixture is cooled to about 25-30 degrees Celsius.

The concentrated solution is then sprayed in a water bath preferably maintained at about 25-30 degrees Celsius, but the temperature of this water bath may be varied from about 5°C to about 85°C to enhance the rate of co-precipitation and to obtain a desired particle size. The water bath also preferably contains a dispersing agent, preferably at a level of about 0.025% w/v to about 15.00% w/v. Preferred dispersing agents herein are surfactants. Without being bound by theory, it is believed that the use of a dispersing agent such as a surfactant in the precipitating medium maintains the agglomeration of the coated dextromethorphan particles minimized to less than about 150 microns.

Non-ionic surfactants are preferred for use herein as the surfactant dispersing agent. An exemplary surfactant suitable for use as the dispersing agent herein is sold by BASF under the trade name LUTROL F 127.

During the spraying of the concentrated alcoholic solution, the water bath is continuously stirred to uniformly disperse the co-precipitate and to prevent settling down prior to surface hardening. The stirring is preferably continued even after spraying is completed to complete the co-precipitation process and the surface hardening. The co-precipitate is filtered and washed with distilled water and dried, for example in an oven, at temperature of about 65 degrees Celsius. The dried material is sieved through a mesh, e.g., a # 60 mesh, to break any lumps formed during drying. According to the coating method described herein, it is believed that at least about 75% of the particles will have a particle size of less than about 90 microns, and at least about 90% of the particles will have a particle size of less than about 150 micron.

The co-precipitate obtained as described above is a composition that is suitable for incorporation as the pharmaceutically active ingredient in medicament compositions, and is particularly desirable for use in the chewable compositions of the present invention. In a preferred embodiment of the present invention, dextromethorphan is present in the co-precipitate at a level of about 47 to about 83%, preferably from about 50 to about 75%.

D. Other Ingredients

In addition to the coated dextromethorphan particles, the compositions of the present invention may desirably include other ingredients, as more fully described below.

1. Thickening Agent

The composition of the present invention may also include a thickening agent. Herein, "thickening agent" refers to a material which provides a desirable consistency when contacted with saliva and/or water in the mouth. Such thickening agents in the composition have characteristics such as wetting quickly and absorbing fluid when contacted with water and/or saliva, thereby swelling and converting into a paste. It is believed that water is absorbed into the structure of the composition maintaining cohesiveness of the composition structure. When more and more water enters the composition structure, more swelling takes place and a paste is formed.

Nonlimiting examples of thickening agents useful herein include: pregelatinized starch; gums such as agars, locust bean gums, guar gums, and tara gums; carrageenan; alginate; xanthan; dextran; and cellulose derivatives such as sodium carboxymethyl cellulose and sodium carboxymethyl hydroxyethyl cellulose. Natural gums such as gum karaya, gum arabic, and gum tragacanth can also be used. Synthetic silicates such as colloidal magnesium aluminum silicate or finely divided silica can be used as part of the thickening agent to further improve texture. The thickening agent is preferably present from about 0.2% to about 5.5% by weight of the composition.

2. Sugar Agent

The composition of the present invention may also include a sugar agent. Herein, "sugar agent" refers to a material which is used to enhance salivation and help in dissolution of the composition. The sugar agent present in the composition can provide sweetness to the formulation, and a desirable dissolution property to the composition as well as aid in the processing of the composition into tablet form. The sugar agent is believed to keep the individual particles of the thickening agent separated and prevent their lumping when contacted with saliva and/or water.

Preferably, the sugar agent useful herein is a sugar, sugar alcohol, or mixture thereof. Nonlimiting examples of sugars useful herein include lactose, glucose, maltodextrins, and sucrose. Sugar alcohols useful herein include sorbitol, xylitol, mannitol and maltitol.

The total amount of sugar agent is selected depending upon its compatibility with the other ingredients, especially drug actives such as dextromethorphan, and the desired characteristic of the composition such as

dissolution and mouthfeel, e.g., bitterness and grittiness of the tablet. The sugar agent is present at an effective level, preferably at a level of from about 20% to about 80%, more preferably from about 20% to about 65% by weight.

Preferably, the sugar agent of the present invention is a combination of sugar and sugar alcohol, more preferably the ratio of sugar of such combination is lower than the ratio of sugar alcohol. A preferred combination is sucrose (sugar) with a higher ratio of mannitol (sugar alcohol). It is believed the combination of sugar and sugar alcohol as the sugar agent improves the pleasant dissolution provided by the combination of the sugar agent with thickening agent. Inclusion of mannitol slows the dissolution speed of the composition as compared to inclusion of sugar only. Without being bound by theory, it is believed that dissolution of a sugar agent having a faster dissolving speed may cause the formation of a thick film around the individual particles of thickening agents, undissolved sugar agents, and other particles included in the composition. Such a thick film tends to prevent further penetration of water into the composition structures and particles which have not dissolved yet; thereby preventing complete and/or even dissolution of the composition as a whole.

Preferably, the composition includes from about 1.0 to about 50% of sugar and from about 20 to about 80% of sugar alcohol by weight of the composition.

In one embodiment, the sugar agent may further include a binding agent. Inclusion of the binding agent is particularly useful when a sugar agent, such as mannitol, may have a limited ability to bind the components used for the composition. It is believed that insufficiencies in binding ability tend to cause tablets to break off, e.g., into two pieces along the length of the tablet during the manufacturing process. This splitting of the tablet is commonly referred to as "capping." The levels and types of binding agent are selected depending upon the character of the carriers, compatibility with other components, and desired characteristic of the final product.

In addition, when the composition is in tablet form, it is recognized that some sugar agent of the present invention may also have properties as a binding agent for making tablets. Most of the sugar agents herein, preferably sugar, may be useful for providing improved binding properties of the composition in tablet form to prevent the tablet from breaking into two pieces.

Examples of useful binding agents, other than the previously described sugar agents, include starches such as starch paste and pregelatinized starch;

polyvinylpyrrolidone; cellulose derivatives; gelatin; gums; and mixtures thereof. In certain embodiments, the binding agent and the tableting carrier may be made of the same material. Alternatively, the binding agent and the sugar agent may be altogether different. The binding agent is present in an effective amount, preferably from about 0.1% to about 5% by weight, more preferably from about 0.5% to about 3%.

3. Water insoluble diluent

The composition of the present invention can further include a water insoluble diluent. Herein, "water insoluble diluent" means a material which improves the disintegration or dispersion property of the tablet composition. Without being bound by theory, it is believed that the water insoluble diluent tends to provide a desired porosity to the composition. Such porosity is believed to provide channels for water into the tablet structure, thereby allowing penetration of, and more exposure of the composition surface area to, the water. The water insoluble diluent useful herein is any material which is insoluble in water which improves the dissolution of the composition, versus a composition that does not contain the material. The water insoluble diluent useful herein includes, but is not limited to, calcium carbonate, calcium phosphate, and the like. Preferably, the water insoluble diluent is present at an effective level, preferably at a level of from about 0.5% to about 70% of the tablet composition.

4. Tableting carrier

The composition of the present invention can further include a tableting carrier. Herein, "tableting carrier" means one or more compatible solid or liquid substances, preferably in solid form, which are suitable for oral administration to a human and commonly used for making tablets. The tableting carrier must be of sufficiently high purity and sufficiently low toxicity to render the tablet suitable for administration to human beings. Examples of useful tableting carriers include the water insoluble diluent, a tableting aid, a coloring agent, a flavoring agent, the granulating fluid, and mixtures thereof. Preferably, the tableting carrier is present from about 10 to about 80%, more preferably from about 30 to about 80% by weight.

a. Tableting aid

Herein, "tableting aid" refers to an ingredient that is added in small quantities to the composition to provide flowability during manufacturing, to reduce friction, and/or to ease removal of the tablets from the tableting machine.

The tableting aids useful herein include, for example, magnesium stearate, stearic acid, aerosol, talc, and mixtures thereof. Preferably, the tableting aid is present in an amount sufficient to prevent the tablet from breaking into two pieces, preferably from about 2% to about 8%, by weight.

b. Coloring agent

The tablet composition of the present invention may further include a coloring agent. Preferably, the coloring agent is added with the granulating fluid to facilitate uniform distribution and mixing. The coloring agent is present at an effective level, preferably from about 10ppm to about 500ppm, more preferably from about 20ppm to about 250ppm by weight.

c. Flavoring agent

Flavoring agents may also be added to the tablet composition of the present invention. Examples of flavoring agents useful herein include oil of peppermint, oil of sassafras, clove bud oil, peppermint, menthol, anethole, thymol, methyl salicylate, eucalyptol, cassia, 1-menthyl acetate, sage, eugenol, parsley oil, oxanone, oil of wintergreen, alpha-irisone, oil of spearmint, marjoram, lemon, orange, propenyl guaethol, cinnamon, and mixtures thereof. Flavoring agents are generally used in the tablet composition at levels of from about 0.01% to about 5% by weight.

The tablet composition in accordance with the present invention may further, optionally, include other known compounds having the capability to enhance substantivity of a sweetener, if desired. These compounds is added to increase the overall sweetness impact. Such compounds include, but are not limited to, saccharine, aspartame, acesulfame K, and glycyrrhizin.

E. Method for Making Tablets

The composition of the present invention in tablet form can be produced by any method useful for forming conventional tablets known in the art. These conventional methods include granulating methods: either wet or dry granulating method, preferably wet granulating. Depending on the properties of the ingredients (e.g., the dextromethorphan, additional drug resin complexes if any, thickening agents, pharmaceutically acceptable carriers, flavors, coloring agents, and the like) to be formulated into granules, one method may provide a more favorable end product over the other method. The wet granulation method is widely used and usually produces the most satisfactory results in tablets. See, for example, E.J. de Jong; "The preparation of microgranulates, an improved

tableting technique," Pharmaceutical Weekblad, 104(23), pages 469-474, 1969 and E.J. de Jong, U.S. Patent 3,266,992.

Direct compression may also be chosen for the present composition, as long as producing non-gritty tablets does not cause capping. See, for example, Blaaze, T. Palermo, et al., U.S. Patent 3,384,546.

In one preferred embodiment of the present invention, a method for making a composition in tablet form comprises: (1) adding the coated dextromethorphan composition prepared as described above, sugar agents and any additional ingredients which are stable in the proceeding process (e.g., coloring agent), if needed, to make granules; (2) passing the granules through #10 mesh; (3) drying the sieved granules through conventional drying techniques; (4) sieving again the dried granules through #14 mesh; (5) mixing the granules of step (4) with a thickening agent and any additional ingredients (e.g., sweetening agent, flavor, tableting aids); and (6) compressing the mixture of step (5) to form tablets by conventional methods.

EXAMPLES

The following examples further describe and demonstrate embodiments within the scope of the present invention. The examples are given solely for the purpose of illustration and are not to be construed as limitations of the present invention, as many variations thereof are possible without departing from the spirit and scope of the invention.

Method of Preparation of Co-Precipitate Composition

The co-precipitate composition as shown below is suitably prepared as follows. The dextromethorphan and the coating agent are dissolved in ethyl alcohol in the quantity mentioned in the table. This mixture is concentrated to 20 ml on a hot water bath. The solution is then sprayed in a water bath containing the dispersing agent. The co-precipitate formed is washed with de-ionized water and dried.

Table 1: Co-precipitate Composition

Components	Ex. 1	Ex. 2	Ex. 3	Ex. 4	Ex. 5
Dextromethorphan	5.0g	5.0g	5.0g	5.0g	5.0g
Coating Agent *1	0.75g	2.0g	5.0g	3.0g	0.21g
Dispersing Agent w/v *2	0.10	0.25	1.1	1.0	1.0
Ethyl Alcohol	50 ml	50 ml	50 ml	50 ml	50 ml

Definitions

*1 Eudragit E-100 obtained by Rohm Pharma.

*2 Lutrol F 127 obtained by BASF.

The co-precipitate prepared as stated above is desirably used as a component for formation into tablets according to the "Method for Making Tablets" section herein. As exemplified in Table 2, tablets of 1.25 g by weight are punched to provide tablets each containing 30 mg equivalent Dextromethorphan HBr. "Dextromethorphan HBr" amount is a term commonly used in the pharmacopial literature to refer to dosage amounts of dextromethorphan. To determine the equivalent Dextromethorphan HBr amount for a given weight of dextromethorphan, the weight amount of dextromethorphan is multiplied by a factor of 1.295 to arrive at the concentration of Dextromethorphan HBr. The factor of 1.295 is derived from the molecular weight of dextromethorphan as follows:

Weight amount of dextromethorphan ≅ Weight amount of Dex.HBr X 0.772

Table 2: Composition Examples

	%w/w				
Components	Ex.1	Ex.2	Ex.3	Ex.4	Ex.5
Co-precipitate Composition	2.00 *a	2.44 *b	3.48 *c	2.79 *d	1.82 *e
Mannitol	40.56	43.55	71.89	72.51	64.83
Sugar	8.00	8.00	4.15	4.15	10.00
Calcium Carbonate	40.56	36.00	-	-	-
Dicalcium phosphate	-	-	12.50	12.50	12.50
Aspartame	0.58	0.46	0.28	0.35	0.65
Xanthan Gum	1.25	0.10	0.50	0.50	1.25
Carboxymethyl cellulose	2.15	0.15	1.50	1.50	3.25
Synthetic silicate	0.20	4.60	1.0	1.0	1.0
Magnesium stearate	2.00	2.00	2.00	2.00	2.00
Talc	2.50	2.50	2.50	2.50	2.50
Flavor	0.19	0.19	0.19	0.19	0.19
Color	0.01	0.01	0.01	0.01	0.01

*a Contains dextromethorphan and Eudragit E-100 in the proportion 5:0.75

*b Contains dextromethorphan and Eudragit E-100 in the proportion 5:2

*c Contains dextromethorphan and Eudragit E-100 in the proportion 5:5

*d Contains dextromethorphan and Eudragit E-100 in the proportion 5:3

*e Contains dextromethorphan and Eudragit E-100 in the proportion 5:0.21

The dissolution profile of the co-precipitate compositions such as shown in Table 1 and prepared as above may be determined by a standard test method mentioned in US pharmacopoeia using 0.1 N HCl as the dissolution medium. Dissolution profile test results are directly correlated to the bioavailability of the drug. The higher the dissolution rate, the quicker the bioequivalence of the drug. Whenever a medically significant difference in bioavailability is found among identical articles, a dissolution test is used to discriminate among these articles. There is no known bioinequivalence problem with articles where 75% of an article is dissolved in water or acid at 37 degrees Celsius in 45 minutes in the official basket or paddle apparatus operated at the usual speed, that is, USP First case. (Refer U.S.Pharmacopiea 23, page lv-lvi.)

A typical dissolution profile for a co-precipitate prepared according to the present invention is as follows:

Table 3: Dissolution Profile

Time (minutes)	% Dextromethorphan released in 0.1 N HCL
15	94
30	97

The embodiments disclosed and represented by the previous examples have many advantages. For example, they provide a convenient, non-liquid dosage form of dextromethorphan, i.e, a chewable tablet, in which the user does not experience the bitter taste of the dextromethorphan active during the chewing and swallowing of the tablet, and experiences good mouthfeel and dissolution of the tablet without a gritty sensation. The higher concentration of the dextromethorphan active in the present compositions may further be quickly dissolved in the stomach, releasing over 85% of the dextromethorphan active within about 15 minutes.

In addition, it is believed that the compositions of the present invention can contain a higher concentration of the dextromethorphan active in comparison with those included in the conventional oral dosage forms, for example, lozenges available from various manufacturers and chewy squares sold by Warner-Lambert under the tradename "Mediquell". It is believed that the conventional chewable products include only from 2.5 mg to 15 mg of dextromethorphan, while the chewy product is believed to contain only about 15 mg equivalent Dextromethorphan HBr.

It is understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to one skilled in the art without departing from the scope of the present invention.

WHAT IS CLAIMED IS:

1. A composition comprising dextromethorphan particles coated with a polymethacrylate copolymer, the coated particles having a particle size of less than about 150 microns.

2. The composition according to claim 1 wherein the ratio of the dextromethorphan to the polymethacrylate copolymer is from about 3:97 to about 50:50.

3. A granule for compression in the forming of tablets comprising the coated dextromethorphan particles according to claim 1 and at least one pharmaceutically acceptable tableting carrier.

4. A chewable tablet comprising the granules according to claim 3 and at least one other ingredient selected from the group consisting of a thickening agent, a sugar agent, and a tableting carrier.

5. A method for preparing a composition comprising dextromethorphan coated with a polymethacrylate copolymer, comprising the steps of:

(a) dissolving dextromethorphan and polymethacrylate copolymer in a solvent, the ratio of the dextromethorphan to the polymethacrylate copolymer being from about 3:97 to about 50:50;

(b) concentrating the dissolved solution obtained by step (a);

(c) spraying the concentrated solution obtained by step (b) in a water bath maintained at from about 5°C to about 85°C and containing a dispersing agent to obtain a co-precipitate, the co-precipitate having a particle size of less than about 150 microns;

(d) washing and drying the co-precipitate obtained by step (c).

6. The method according to claim 5 wherein the dispersing agent is a surfactant.

7. The method according to claim 6 wherein the surfactant is present in the water bath at a level of from about 0.025% w/v to about 15.00% w/v.

8. The method according to claim 5 further comprising the step of forming the co-precipitate and at least one other ingredient selected from the group consisting of a thickening agent, a sugar agent, and a tableting agent into tablets.

9. A chewable tablet made by the method according to any of claims 5-8.

10. A composition comprising dextromethorphan particles coated with a polymethacrylate copolymer, the coated particles having a particle size of less than about 150 microns; a thickening agent; and a sugar agent; wherein the composition is in solid form, and wherein the combination of the thickening agent and the sugar agent causes the composition to quickly dissolve in the mouth when contacted with saliva.

INTERNATIONAL SEARCH REPORT

Intern. al Application No
PCT/US 98/19943

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K9/00 A61K9/14 A61K9/16 A61K31/485

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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Y	US 5 354 556 A (SPARKS RANDALL T ET AL) 11 October 1994 see the whole document ---	1-10
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

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Date of the actual completion of the international search	Date of mailing of the international search report
26 May 1999	01/06/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Fischer, W

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